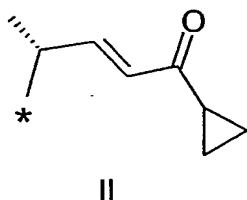
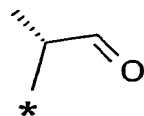


## CLAIMS

1. A method of preparing a compound of general structure II,

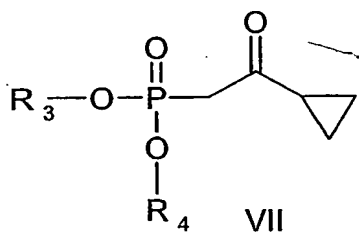


5 wherein the carbon marked with an asterisk is either connected by a single bond to a carbon atom of a vitamin D analogue fragment at C-17 or to a fragment of a precursor for the synthesis of a vitamin D analogue at a C-17 analogous position, the method comprising reacting a compound of general structure IIa,



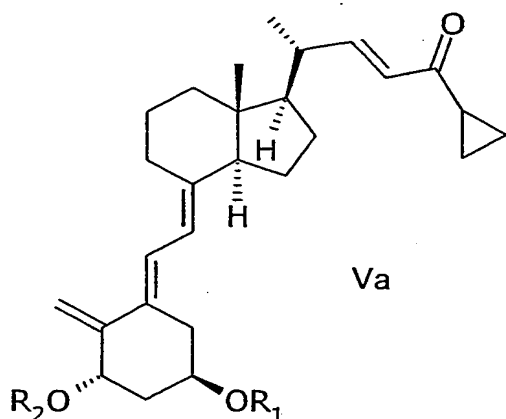
11a

10. wherein the carbon marked with an asterisk is either connected by a single bond to a carbon atom of a vitamin D analogue fragment at C-17 or to a fragment of a precursor for the synthesis of a vitamin D analogue at a C-17 analogous position, with a phosphonate of general structure VII,



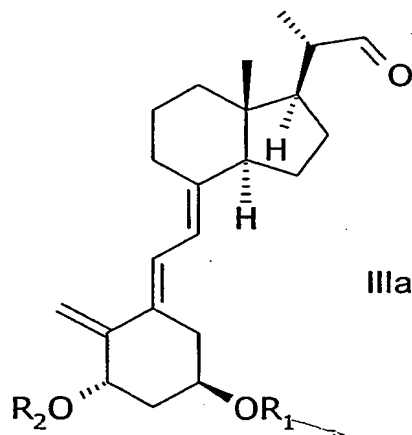
15 wherein R<sub>3</sub> and R<sub>4</sub> are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or  
20 hydroxy,  
in the presence of a base.

2. A method according to claim 1 of preparing a compound of general structure Va,



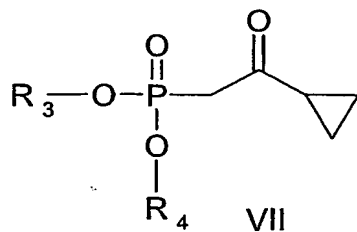
wherein  $R_1$  and  $R_2$  are the same or different and each represent hydrogen or a hydroxy protecting group,

the method comprising reacting a compound of general structure IIIa,



wherein  $R_1$  and  $R_2$  are as defined above,

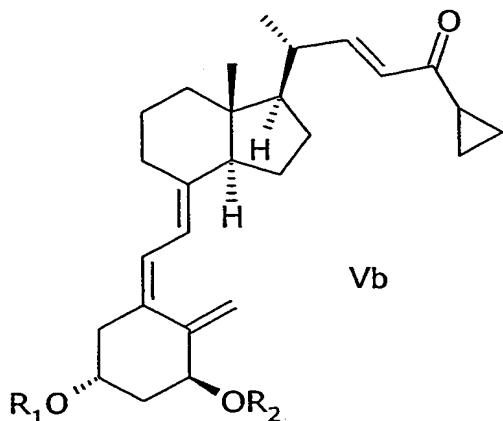
with a phosphonate of general structure VII,



wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy,

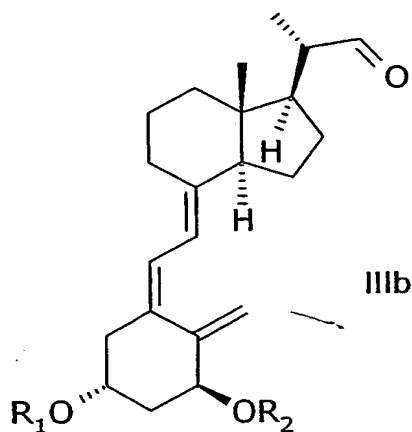
in the presence of a base.

3. A method according to claim 1 of preparing a compound of general structure Vb,

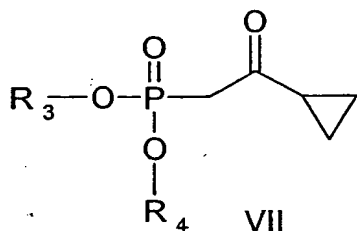


wherein  $R_1$  and  $R_2$  are the same or different and each represent hydrogen or a hydroxy protecting group,

the method comprising reacting a compound of general structure IIIb,



wherein  $R_1$  and  $R_2$  are as defined above,  
with a phosphonate of general structure VII,

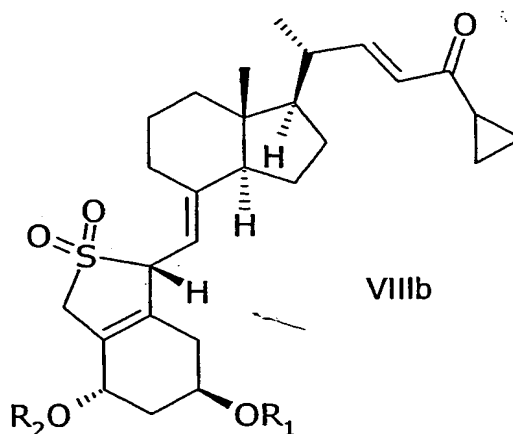
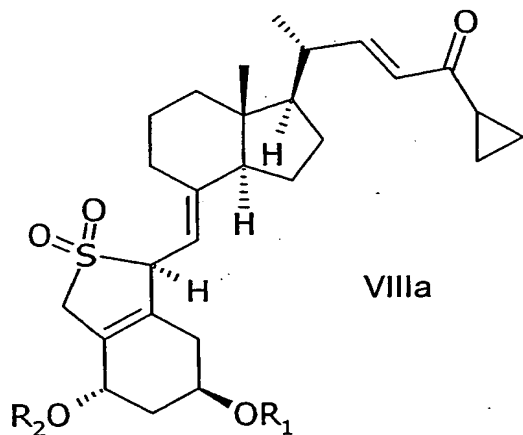


wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl,

aralkynyl, aryl, oxo, alkoxy carbonyl, alkyl carbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy,

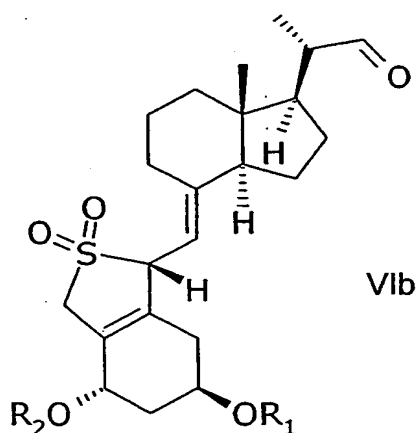
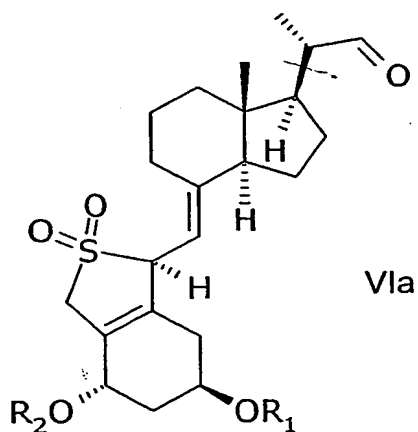
in the presence of a base.

- 5 4. A method according to claim 1 of preparing a compound of general structure VIIIa or VIIIb respectively,

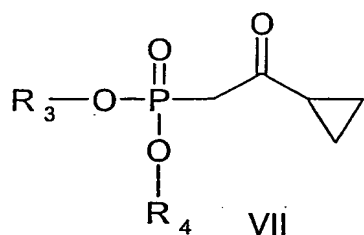


wherein  $R_1$  and  $R_2$  are the same or different and each represent hydrogen or a hydroxy protecting group,

- 10 the method comprising reacting a compound of general structure VIa or VIb respectively,

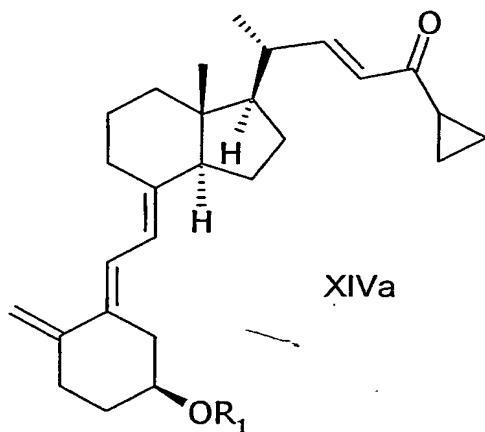


wherein  $R_1$  and  $R_2$  are as defined above,  
with a phosphonate of general structure VII,

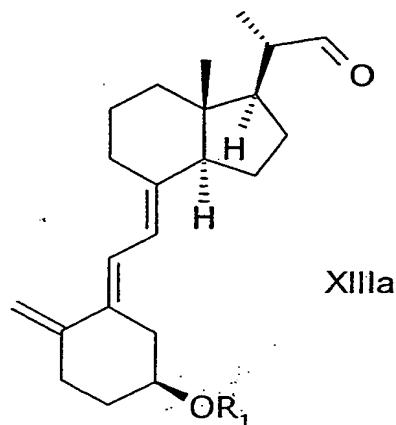


wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxy, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

5. A method according to claim 1 of preparing a compound of general structure XIVa,

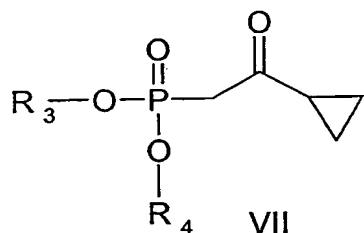


wherein  $R_1$  represents hydrogen or a hydroxy protecting group, the method comprising reacting a compound of general structure XIIIa,



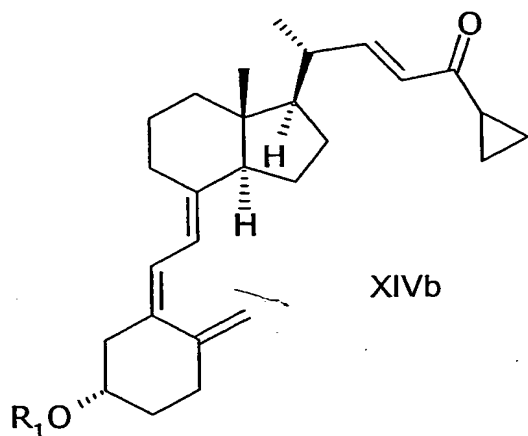
- wherein  $R_1$  is as defined above,

with a phosphonate of general structure VII,

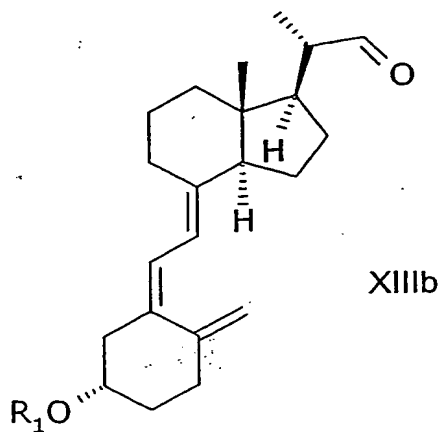


wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, in the presence of a base.

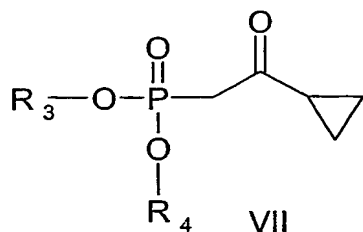
6. A method according to claim 1 of preparing a compound of general structure XIVb,



wherein  $R_1$  represents hydrogen or a hydroxy protecting group, the method comprising reacting a compound of general structure XIIIb,



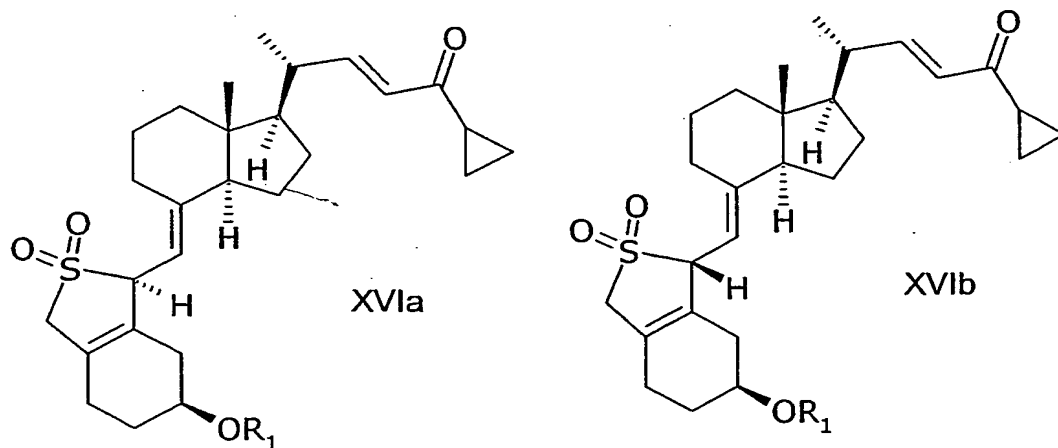
wherein  $R_1$  is as defined above,  
with a phosphonate of general structure VII,



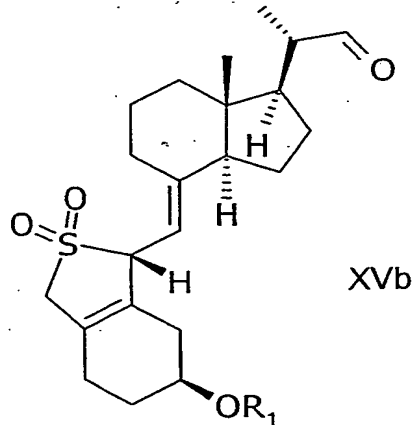
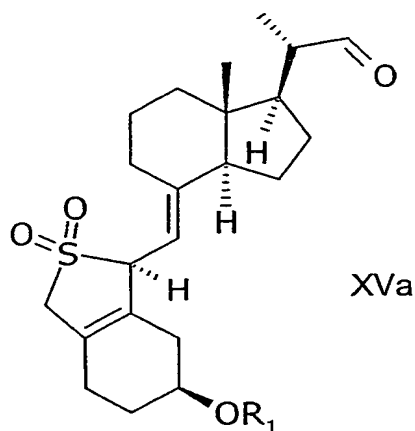
wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy,

in the presence of a base.

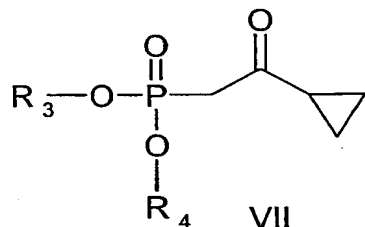
7. A method according to claim 1 of preparing a compound of general structure XVIa or XVIb respectively,



wherein  $R_1$  represents hydrogen or a hydroxy protecting group,  
the method comprising reacting a compound of general structure XVa or XVb respectively,

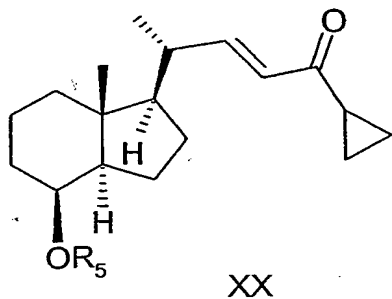


wherein  $R_1$  is as defined above,  
with a phosphonate of general structure VII,

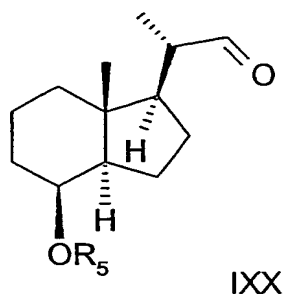


- 5 wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or  
10 hydroxy,  
in the presence of a base.

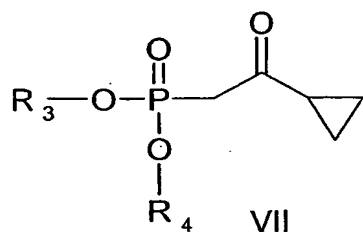
8. A method according to claim 1 of preparing a compound of general structure XX,



- 15 wherein  $R_5$  represents hydrogen or a hydroxy protecting group,  
the method comprising reacting a compound of general structure IXX,



wherein R<sub>5</sub> is as defined above,  
with a phosphonate of general structure VII,



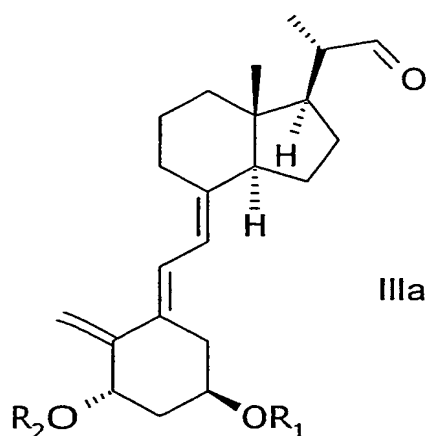
- 5 wherein R<sub>3</sub> and R<sub>4</sub> are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxy, carbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or
- 10 hydroxy,  
in the presence of a base.

9. A method of preparing calcipotriol or calcipotriol monohydrate, the method comprising the method according to any one of claims 1, 2, 3, 4, 5, 6, 7, or 8.

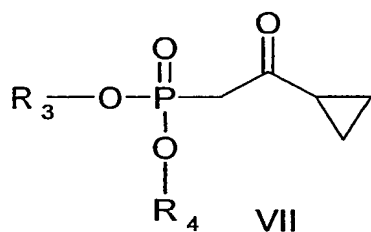
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10. A method for producing calcipotriol or calcipotriol monohydrate, the method comprising the steps of:

(i) reacting a compound of general structure IIIa,



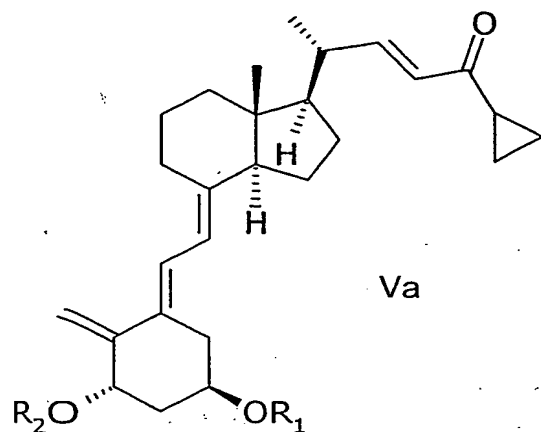
wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group,  
with a phosphonate of general structure VII,



wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy,

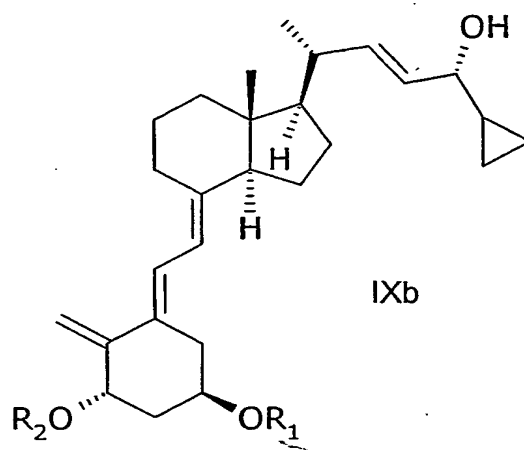
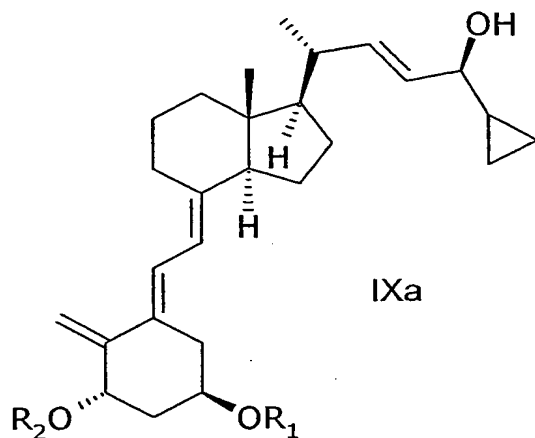
in the presence of a base,

to give a compound of general structure Va,



wherein  $R_1$  and  $R_2$  are as defined above;

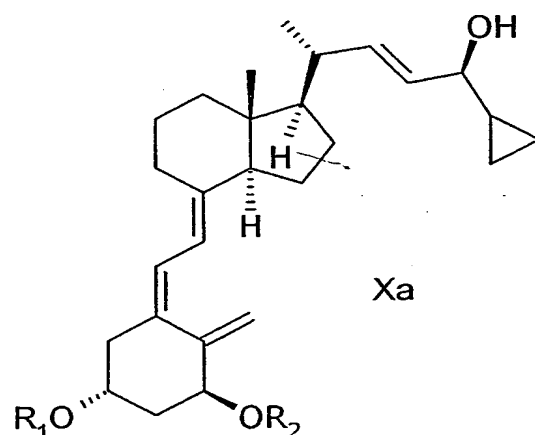
(ii) reducing the compound of general structure Va with a suitable reducing agent, to give a compound of general structure IXa or a mixture of compounds of general structure IXa and IXb,



5 wherein  $R_1$  and  $R_2$  are as defined above;

(iii) optionally separating the compound of general structure IXa from the mixture of compounds of general structure IXa and IXb;

(iv) photoisomerising the compound of general structure IXa to the compound of general structure Xa,



10

wherein  $R_1$  and  $R_2$  are as defined above;

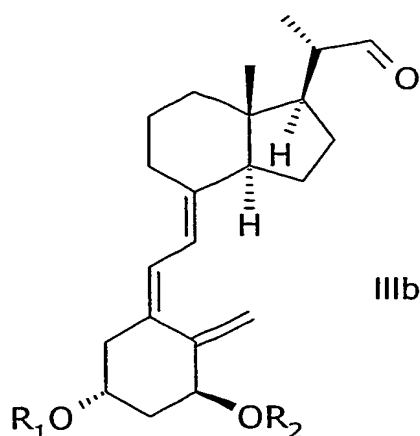
(v) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and

(vi) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.

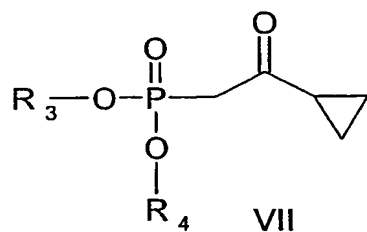
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11. A method for producing calcipotriol or calcipotriol monohydrate, the method comprising the steps of:

(i) reacting a compound of general structure IIb,

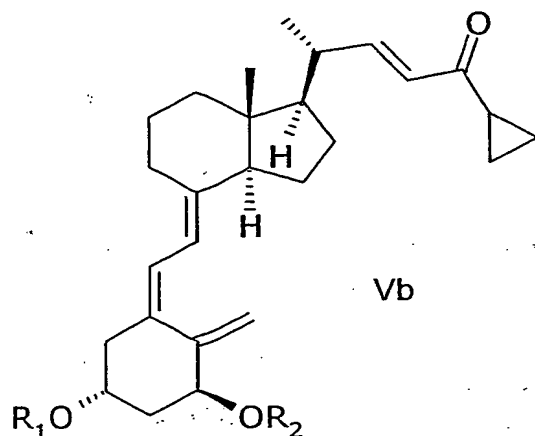


wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group,  
with a phosphonate of general structure VII,



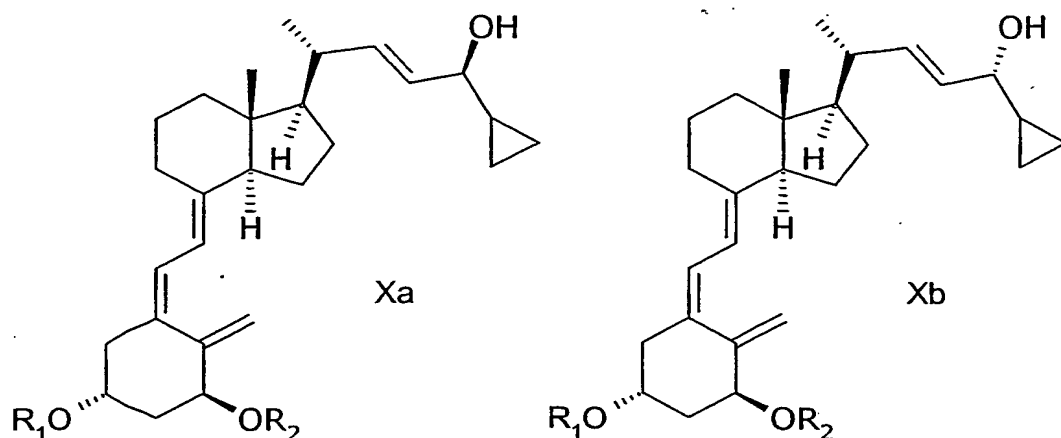
wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy,

in the presence of a base,  
to give a compound of general structure Vb,



wherein  $R_1$  and  $R_2$  are as defined above;

(ii) reducing the compound of general structure Vb with a suitable reducing agent, to give a compound of general structure Xa or a mixture of compounds of general structure Xa and Xb,



5 wherein  $R_1$  and  $R_2$  are as defined above;

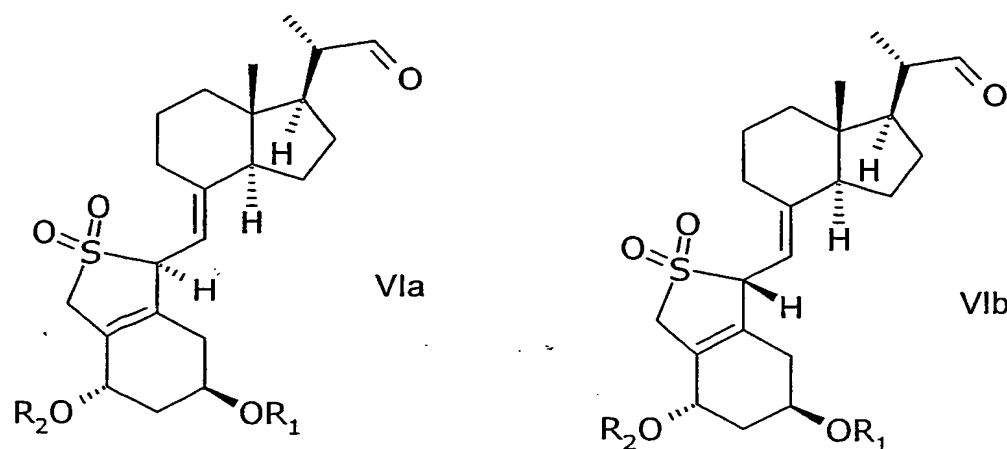
(iii) optionally separating the compound of general structure Xa from the mixture of compounds of general structure Xa and Xb;

(iv) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and

10 (v) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.

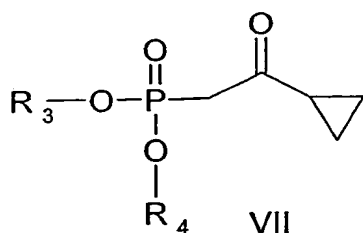
12. A method for producing calcipotriol or calcipotriol monohydrate, the method comprising the steps of:

15 (i) reacting a compound of general structure VIa and/or VIb,



wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group,

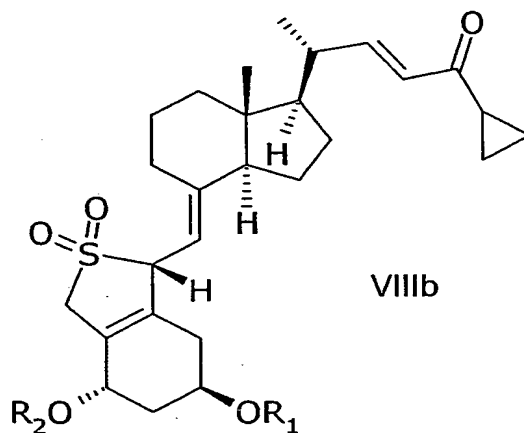
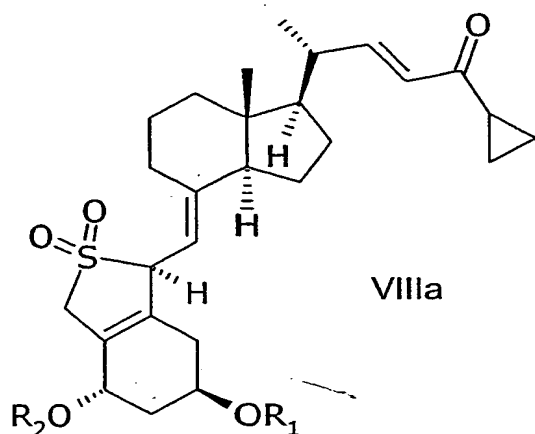
with a phosphonate of general structure VII,



wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxy, carbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy,

in the presence of a base,

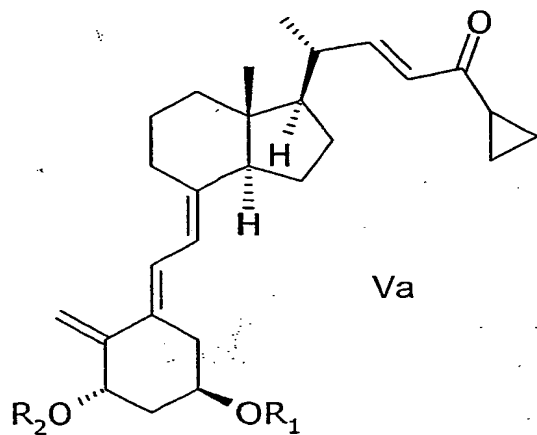
to give a compound of general structure VIIIa and/or VIIIb,



wherein  $R_1$  and  $R_2$  are as defined above;

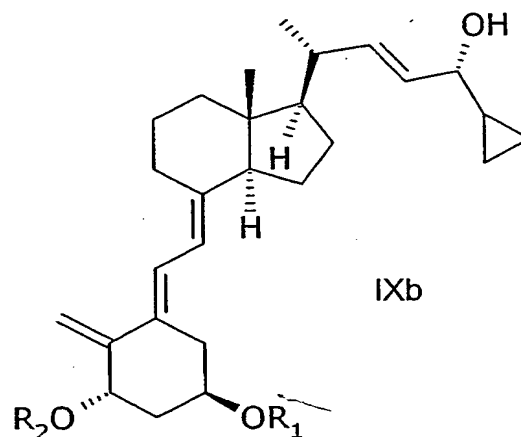
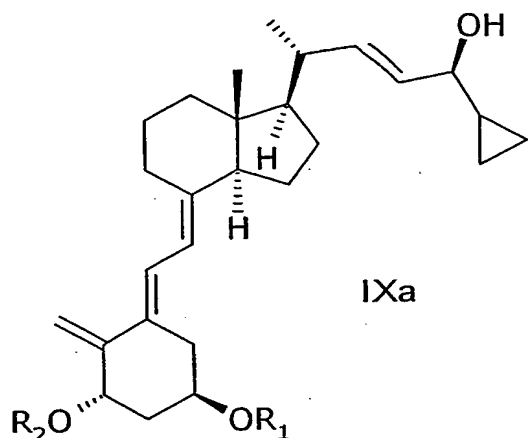
(ii) heating the compounds of general structure VIIIa and/or VIIIb above 60°C in the presence of a base,

to give a compound of general structure Va,



wherein  $R_1$  and  $R_2$  are as defined above;

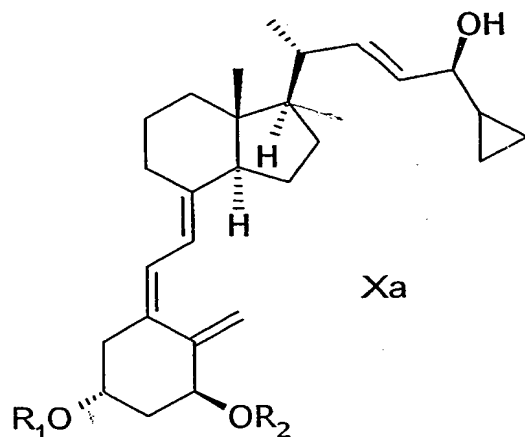
(iii) reducing the compound of general structure Va with a suitable reducing agent, to give a compound of general structure IXa or a mixture of compounds of general structure IXa and IXb,



wherein  $R_1$  and  $R_2$  are as defined above;

(iv) optionally separating the compound of general structure IXa from the mixture of compounds of general structure IXa and IXb;

(v) photoisomerising the compound of general structure IXa to the compound of general structure Xa,



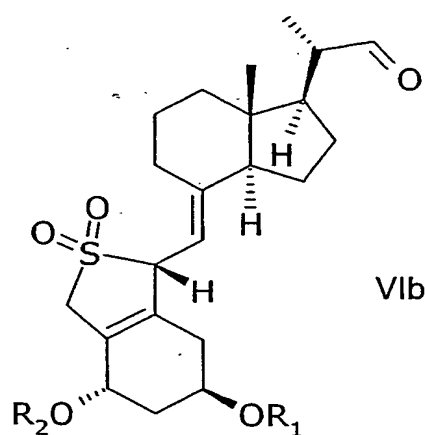
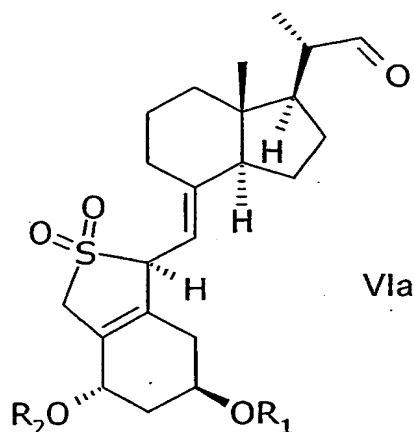
wherein  $R_1$  and  $R_2$  are as defined above;

(vi) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and

(vii) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.

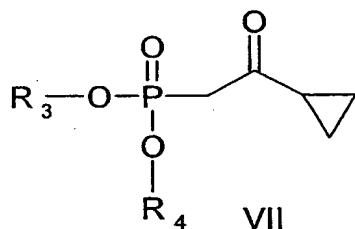
13. A method for producing calcipotriol or calcipotriol monohydrate, the method comprising the steps of:

(i) reacting a compound of general structure VIa and/or VIb,



wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group,

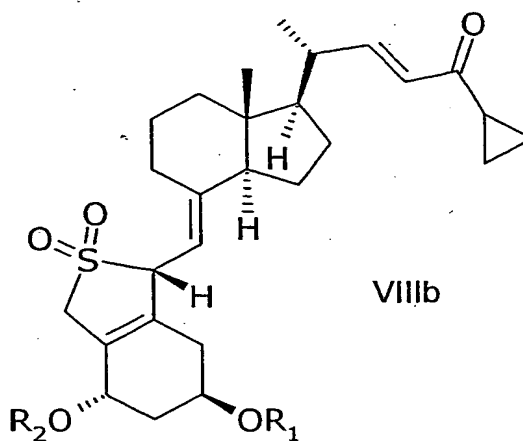
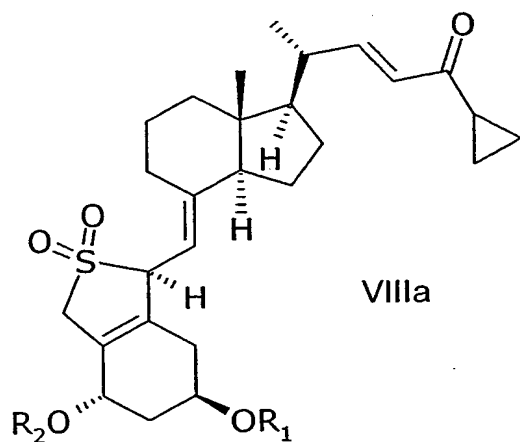
5 with a phosphonate of general structure VII,



wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxy, alkoxy, carboxy, sulfo or hydroxy,

10 in the presence of a base,

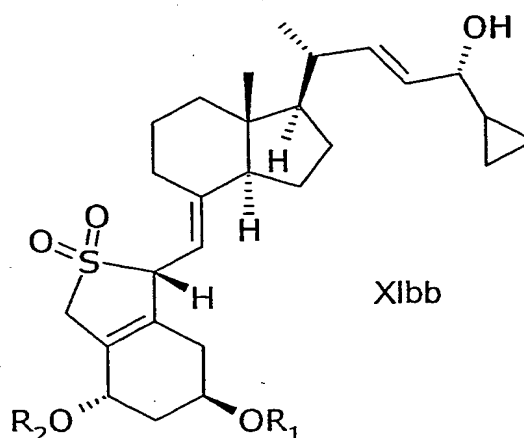
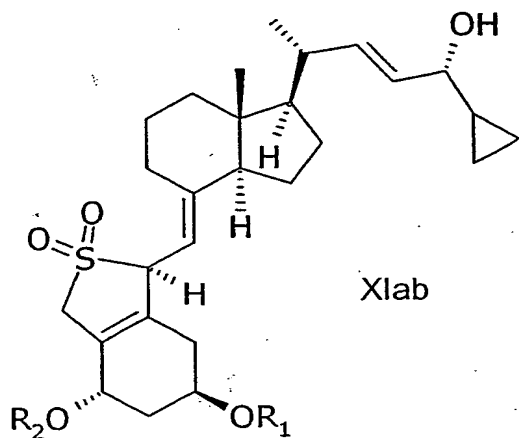
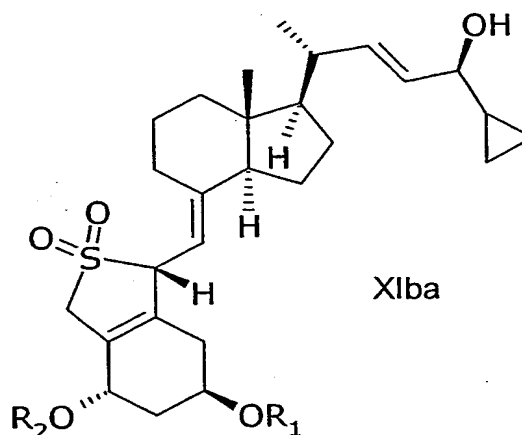
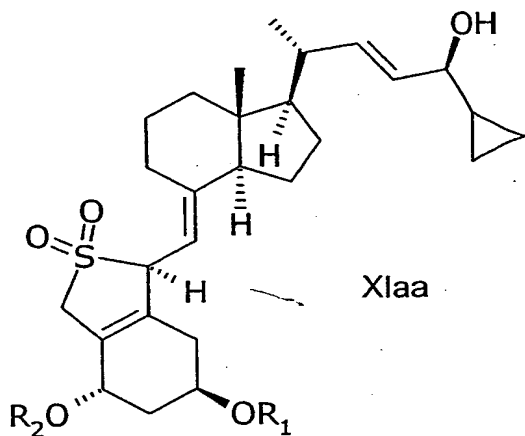
to give a compound of general structure VIIIa and/or VIIIb,



wherein  $R_1$  and  $R_2$  are as defined above;

(ii) reducing the compounds of general structure VIIIa and/or VIIIb, with a suitable reducing agent in an inert solvent,

- 5 to give compounds of general structure XIa and/or XIb, or a mixture of compounds of general structure XIa and/or XIb and XIab and/or XIbb,



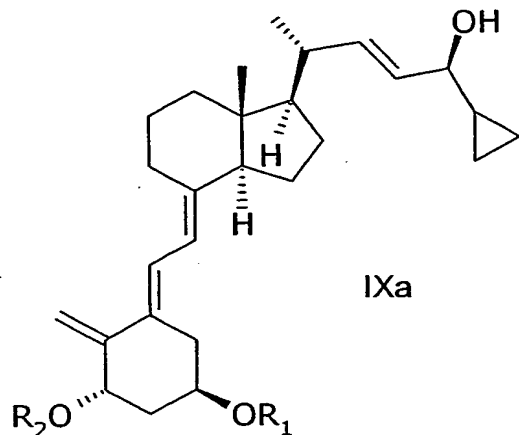
wherein  $R_1$  and  $R_2$  are as defined above;

(iii) optionally separating the compounds of general structure XIaa and/or XIba from the reaction mixture;

(iv) heating the compounds of general structure XIaa and/or XIba above 60°C in the

5 presence of a base,

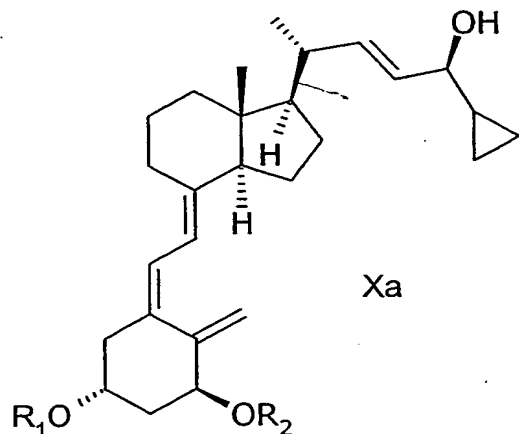
to give a compound of general structure IXa,



wherein  $R_1$  and  $R_2$  are as defined above;

(v) optionally separating the compound of general IXa from the reaction mixture;

10 (vi) photoisomerising the compound of general structure IXa to the compound of general structure Xa,



wherein  $R_1$  and  $R_2$  are as defined above;

(vii) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and

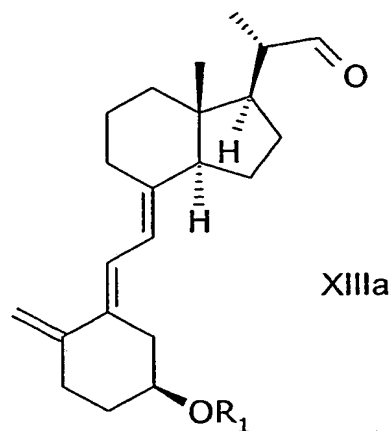
15

(viii) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate;

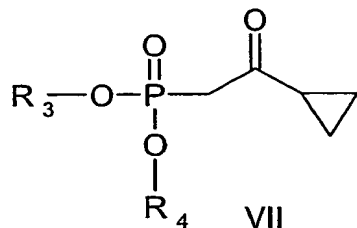
wherein steps (vi) and (vii) may be in reversed order.

14. A method for producing calcipotriol or calcipotriol monohydrate, the method comprising the steps of:

(i) reacting a compound of general structure XIIIa,



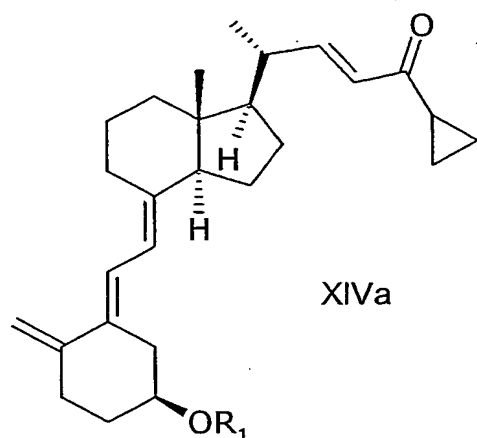
5 wherein R<sub>1</sub> represents hydrogen or a hydroxy protecting group,  
with a phosphonate of general structure VII,



wherein R<sub>3</sub> and R<sub>4</sub> are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy,

in the presence of a base,

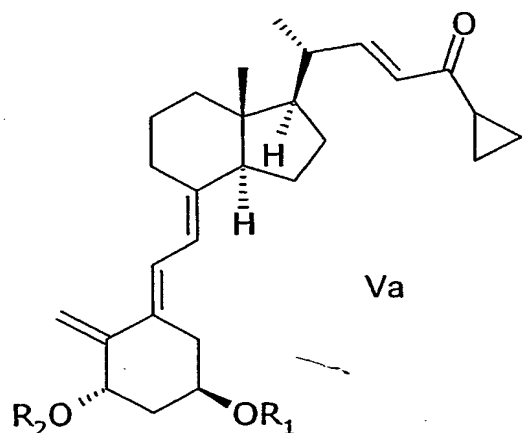
15 to give a compound of general structure XIVa,



wherein  $R_1$  is as defined above;

(ii) hydroxylating the compound of general structure XIVa with suitable hydroxylating agent,

5 to give a compound of general structure Va,



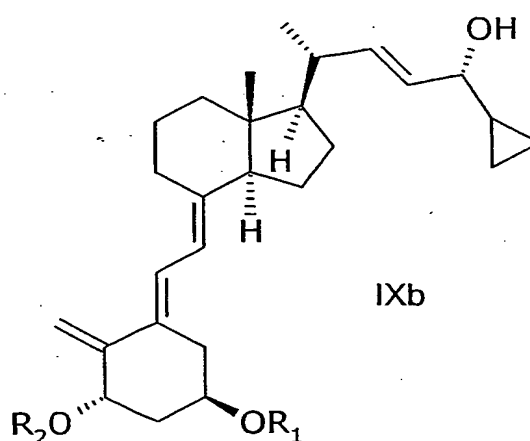
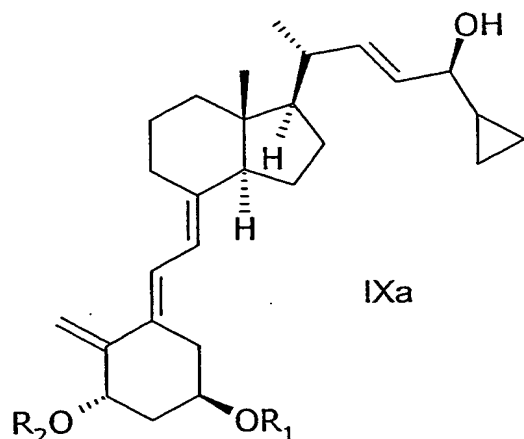
wherein  $R_1$  represents hydrogen or a hydroxy protecting group and  $R_2$  is hydrogen;

(iii) optionally reacting the compound of general structure Va, wherein  $R_1$  represents hydrogen or a hydroxy protecting group and  $R_2$  is hydrogen with a suitable protecting agent,

10 to give a compound of general structure Va, wherein  $R_1$  and  $R_2$  are the same or different and represent a hydroxy protecting group;

(iv) reducing the compound of general structure Va with a suitable reducing agent, to give a compound of general structure IXa or a mixture of compounds of general structure IXa and IXb,

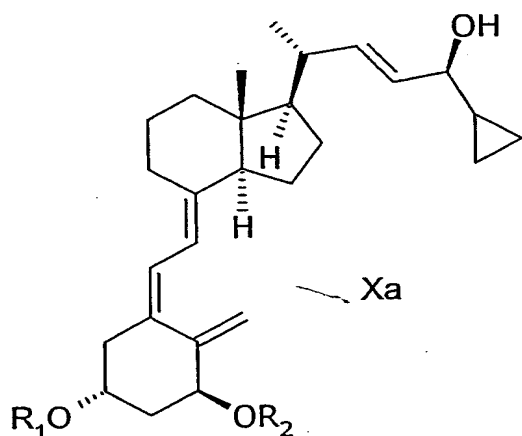
15



wherein  $R_1$  and  $R_2$  are as defined above;

(v) optionally separating the compound of general structure IXa from the mixture of compounds of general structure IXa and IXb;

- 5 (vi) photoisomerising the compound of general structure IXa to a compound of general structure Xa,

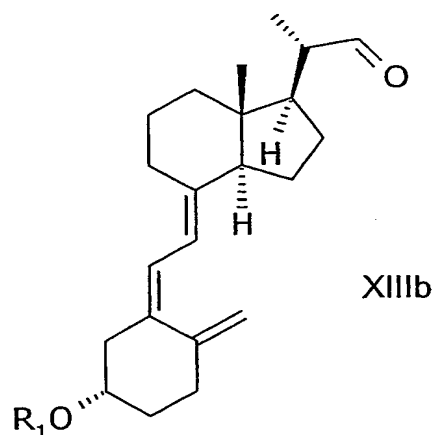


wherein  $R_1$  and  $R_2$  are as defined above;

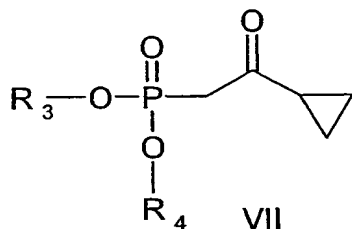
- 10 (vii) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and  
 (viii) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.

- 15 15. A method for producing calcipotriol or calcipotriol monohydrate, the method comprising the steps of:

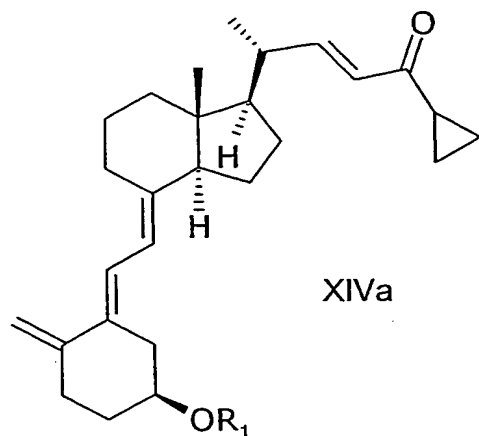
(i) reacting a compound of general structure XIIIb,



wherein  $R_1$  represents hydrogen or a hydroxy protecting group,  
with a phosphonate of general structure VII,



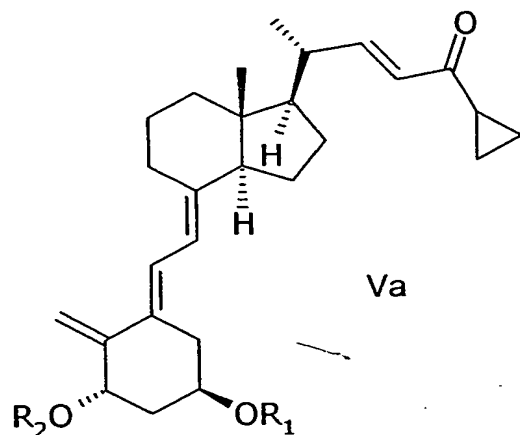
- 5 wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or
- 10 hydroxy,  
in the presence of a base,  
to give a compound of general structure XIVb,  
wherein  $R_1$  is as defined above;
- (ii) photoisomerising the compound of general structure XIVb to a compound of general
- 15 structure XIVa,



wherein  $R_1$  is as defined above;

(iii) hydroxylating the compound of general structure XIVa with suitable hydroxylating agent,

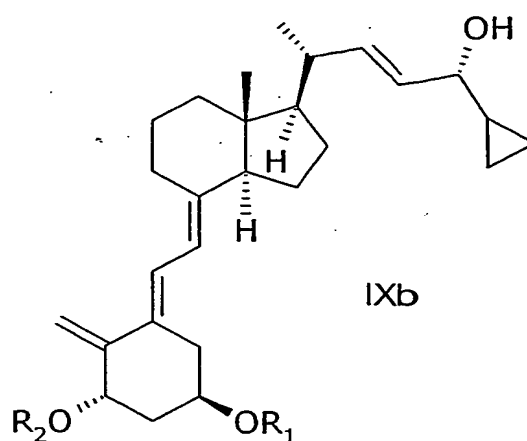
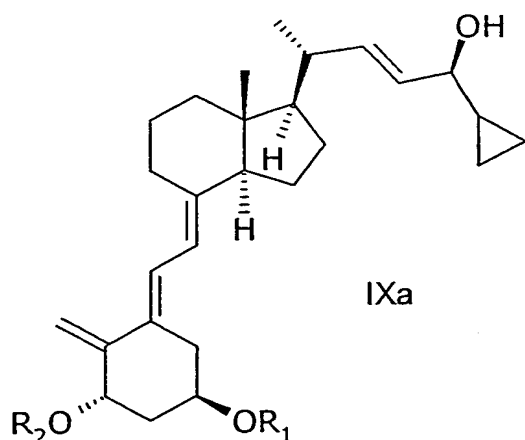
5 to give a compound of general structure Va,



wherein  $R_1$  represents hydrogen or a hydroxy protecting group and  $R_2$  is hydrogen;

(iv) optionally reacting the compound of general structure Va, wherein  $R_1$  represents hydrogen or a hydroxy protecting group and  $R_2$  is hydrogen with a suitable protecting agent to give a compound of general structure Va, wherein  $R_1$  and  $R_2$  are the same or different and represent a hydroxy protecting group;

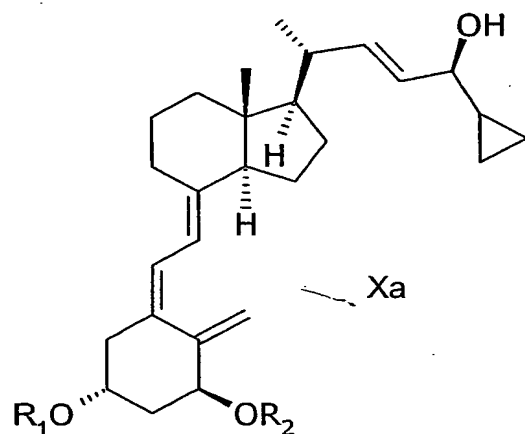
(v) reducing the compound of general structure Va with a suitable reducing agent, to give a compound of general structure IXa or a mixture of compounds of general structure IXa and IXb,



wherein  $R_1$  and  $R_2$  are as defined above;

(vi) optionally separating the compound of general structure IXa from the mixture of compounds of general structure IXa and IXb;

- 5 (vii) photoisomerising the compound of general structure IXa to the compound of general structure Xa,

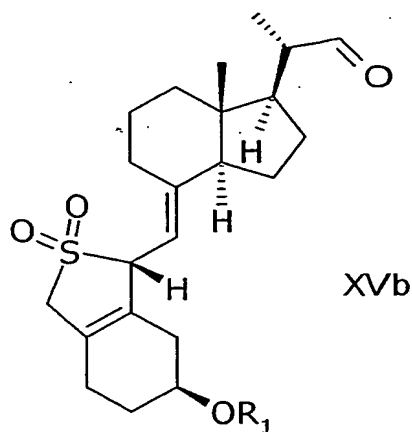
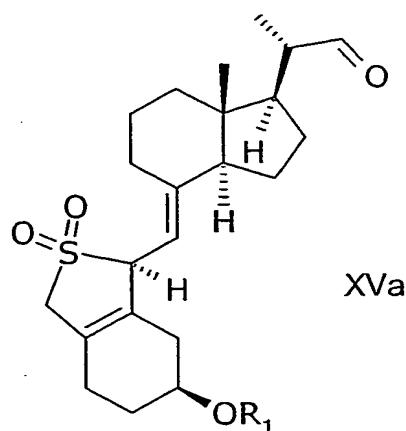


wherein  $R_1$  and  $R_2$  are as defined above;

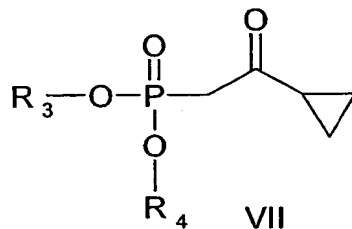
- 10 (viii) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and  
 (ix) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.

- 15 16. A method for producing calcipotriol or calcipotriol monohydrate, the method comprising the steps of:

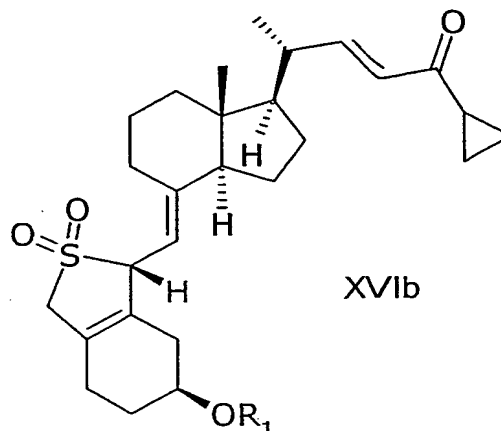
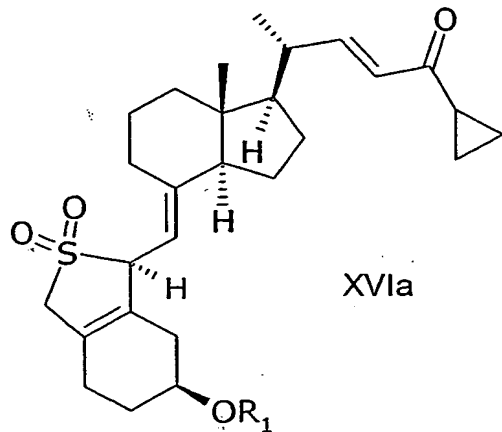
(i) reacting a compound of general structure XVa and/or XVb,



wherein  $\text{R}_1$  represents a hydrogen or a hydroxy protecting group, with a phosphonate of general structure VII,

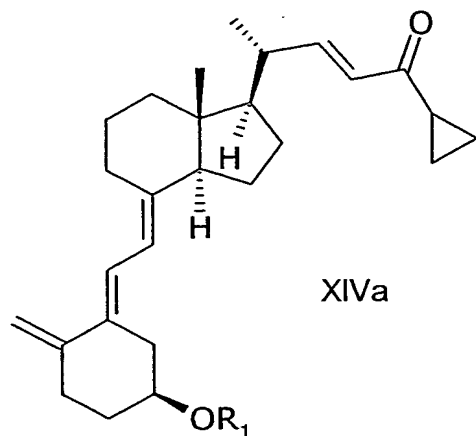


- 5 wherein  $\text{R}_3$  and  $\text{R}_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or
- 10 hydroxy, in the presence of a base, to give a compound of general structure XVIa and/or XVIb,



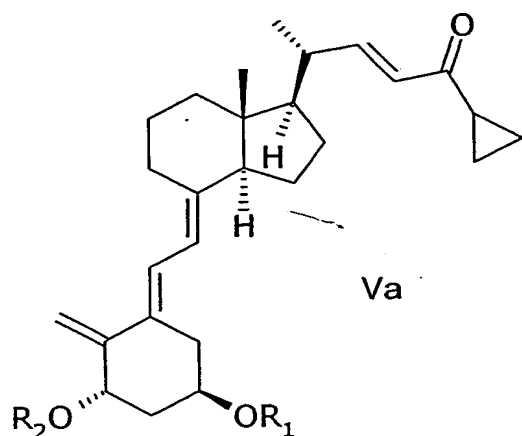
wherein  $\text{R}_1$  is as defined above;

(ii) heating the compounds of general structure XVIa and/or XVIb above 60°C in the presence of a base,  
to give a compound of general structure XIVa,



5 wherein  $R_1$  is as defined above;

(iii) hydroxylating the compound of general structure XIVa with suitable hydroxylating agent,  
to give a compound of general structure Va,



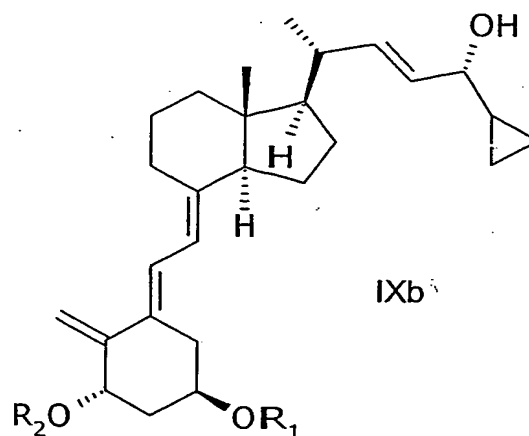
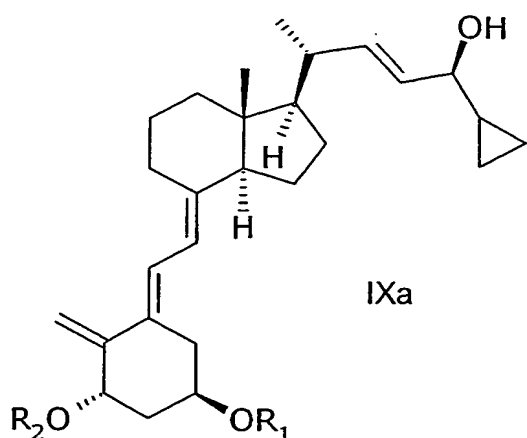
10 wherein  $R_1$  represents hydrogen or a hydroxy protecting group and  $R_2$  is hydrogen;

(iv) optionally reacting the compound of general structure Va, wherein  $R_1$  represents hydrogen or a hydroxy protecting group and  $R_2$  is hydrogen with a suitable protecting agent,

to give a compound of general structure Va, wherein  $R_1$  and  $R_2$  are the same or different

15 and represent a hydroxy protecting group;

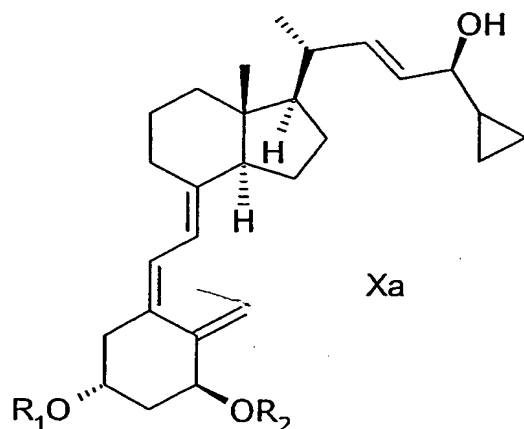
(v) reducing the compound of general structure Va with a suitable reducing agent,  
to give a compound of general structure IXa or a mixture of compounds of general structure IXa and IXb,



wherein  $R_1$  and  $R_2$  are as defined above;

(vi) optionally separating the compound of general structure IXa from the mixture of compounds of general structure IXa and IXb;

- 5 (vii) photoisomerising the compound of general structure IXa to the compound of general structure Xa,

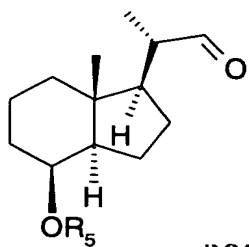


wherein  $R_1$  and  $R_2$  are as defined above;

- (viii) when  $R_1$  and/or  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and/or  $R_2$  of the compound of general structure Xa to generate calcipotriol; and
- 10 (ix) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.

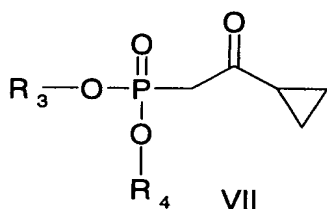
- 15 17. A method for producing calcipotriol or calcipotriol monohydrate, the method comprising the steps of:

(i) reacting a compound of general structure IXX,



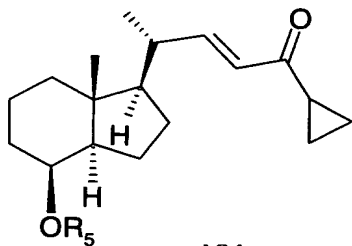
IXX

wherein  $R_5$  represents hydrogen or a hydroxy protecting group,  
with a phosphonate of general structure VII,



VII

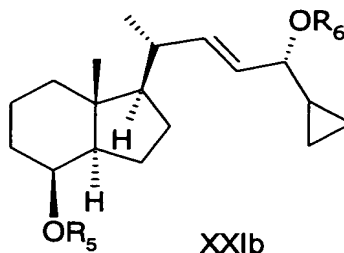
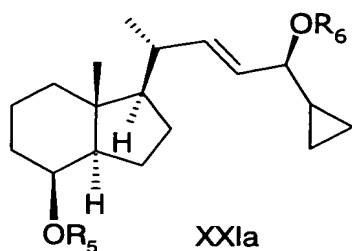
- 5 wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or
- 10 hydroxy,  
in the presence of a base,  
to give a compound of general structure XX,



XX

wherein  $R_5$  is as defined above;

- 15 (ii) reducing the compound of general structure XX with a suitable reducing agent,  
to give a compound of general structure XXIa or a mixture of compounds of general structure XXIa and XXIb,



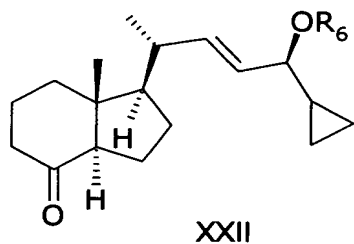
wherein  $R_5$  is as defined above and  $R_6$  is hydrogen;

(iii) optionally separating the compound of general structure XXIIa from the mixture of compounds of general structure XXIIa and XXIIb;

- 5 (iv) protecting the allylic hydroxy group of the compound of general structure XXIIa with a suitable hydroxy protecting reagent, to give a compound of general structure XXIIa, wherein  $R_6$  is a hydroxy protecting group and  $R_5$  is as defined above;

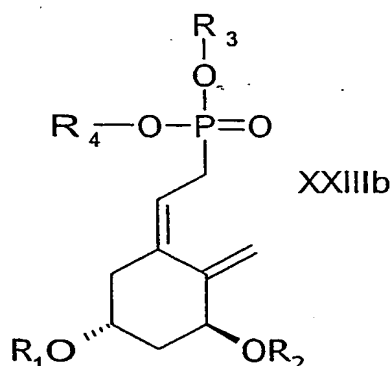
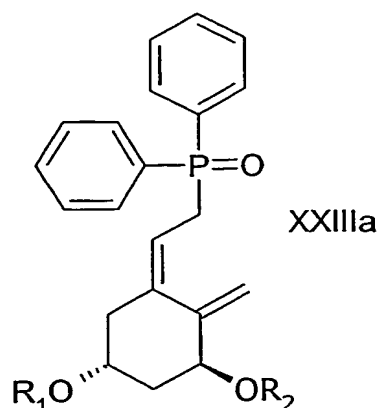
- (v) when  $R_5$  is not hydrogen, removing the hydroxy protecting group  $R_5$  of the compound of general structure XXIIa to give a compound of general structure XXIIa, wherein  $R_5$  is hydrogen;
- 10

(vi) oxidising the hydroxy group of the compound of general structure XXIIa with a suitable oxidising agent to give a compound of general structure XXII,



- 15 wherein  $R_6$  is as defined above;

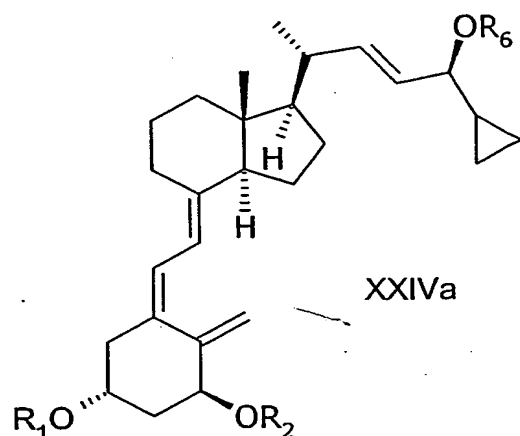
(vii) coupling of the compound of general structure XXII with a Wittig reagent XXIIIa or a Wittig Horner reagent XXIIIb,



wherein  $R_1$  and  $R_2$  represent a hydrogen or a hydroxy protecting group, and wherein  $R_3$  and  $R_4$  are as defined above;

in the presence of a base,

5 to give a compound of general structure XXIVa,



wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group, and wherein  $R_6$  is as defined above;

- 10 (viii) when  $R_6$  is not hydrogen, removing the hydroxy protecting group  $R_6$  of the compound of general structure XXIVa;
- (ix) optionally separating the compound of general structure XXIVa;
- (x) when  $R_1$  and  $R_2$  are not hydrogen, removing the hydroxy protecting group(s)  $R_1$  and  $R_2$  of the compound of general structure XXIVa to generate calcipotriol;
- 15 and
- (xi) optionally crystallising the calcipotriol from a mixture of an organic solvent and water to give calcipotriol monohydrate.

18. The method according to any one of claims 1-17, wherein  $R_3$  and  $R_4$  are  $(C_1-C_6)$ alkyl.

19. The method according to any one of claims 1-17, wherein  $R_3$  and  $R_4$  are methyl or ethyl.

20. The method according to any one of claims 1-19, wherein  $R_1$  and  $R_2$  represent hydrogen or alkylsilyl.

21. The method according to any one of claims 1-19, wherein  $R_1$  and  $R_2$  represent hydrogen or *tert*-butyldimethylsilyl.

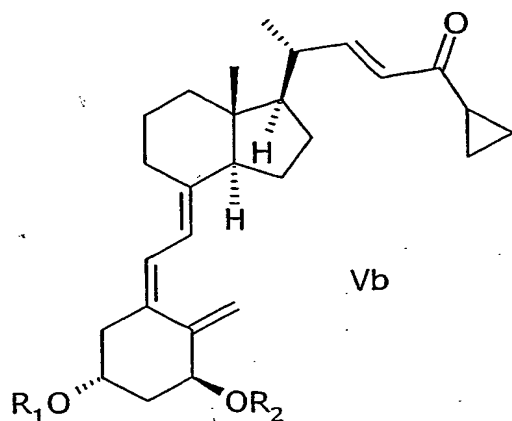
22. The method according to claim 8 or 19, wherein  $R_5$  represents triethylsilyl and  $R_3$  and  $R_4$  are methyl or ethyl.

23. The method according to any one of claims 1-22, wherein the reaction with the phosphonate of general structure VII is carried out under phase-transfer conditions.

24. The method according to any one of claims 1-22, wherein the reaction with the phosphonate of general structure VII is carried out under phase-transfer conditions in a mixture of toluene or xylene and water with a tetraalkylammonium halide or a tetraalkylammonium hydrogensulfate as the phase transfer catalyst and with an alkalimetal hydroxide and/or a tetraalkylammoniumhydroxide as the base.

25. The method according to any one of claims 1-24, wherein the reaction with the phosphonate of general structure VII is carried out at a temperature between 10°C-50°C.

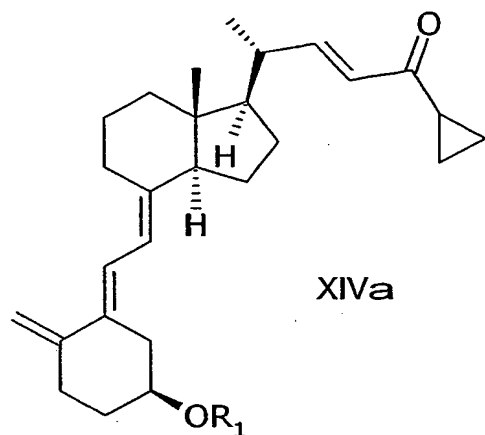
26. A compound of general structure Vb,



wherein  $R_1$  and  $R_2$  are the same or different and each represent a hydroxy protecting group, or  $R_1$  represents hydrogen and  $R_2$  represents a hydroxy protecting group, or  $R_2$  represents hydrogen and  $R_1$  represents a hydroxy protecting group.

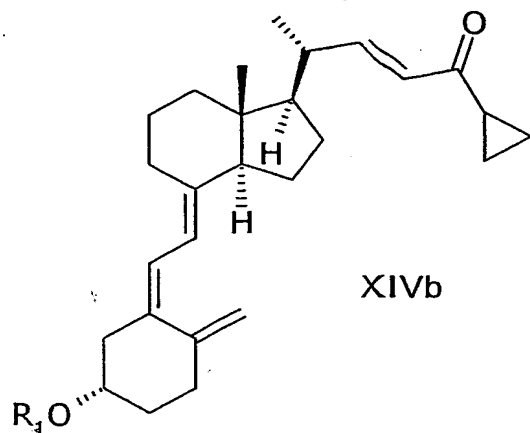
- 5 27. 20(R),1(S),3(R)-bis(*tert*-butyldimethylsilyloxy)-20-(3'-cyclopropyl-3'-oxoprop-1'(E)-enyl)-9,10-secopregna-5(Z),7(E),10(19)-triene.

28. A compound of general structure XIVa,



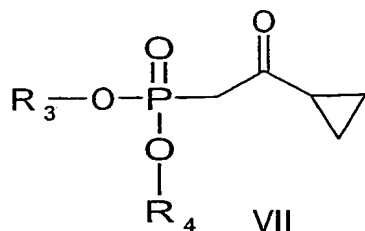
- 10 wherein  $R_1$  represents hydrogen or a hydroxy protecting group, with the proviso that  $R_1$  cannot be *tert*-butyldimethylsilyl.

29. A compound of general structure XIVb,



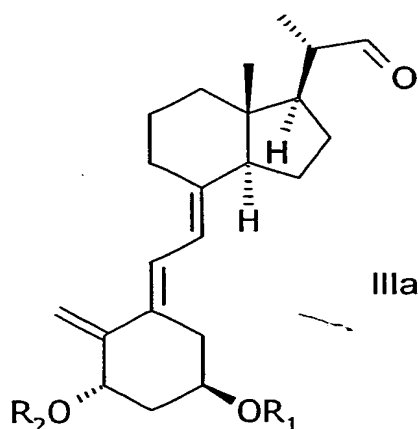
- 15 wherein  $R_1$  represents hydrogen or a hydroxy protecting group.

30. A compound of general structure VII,



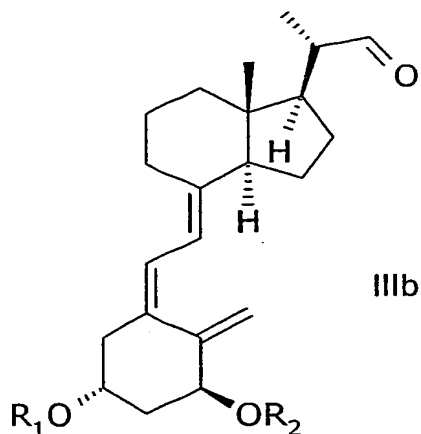
wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy, provided that that the compound is not (2-cyclopropyl-2-oxoethyl)phosphonic acid diethyl ester.

31. A compound of general structure IIIa,



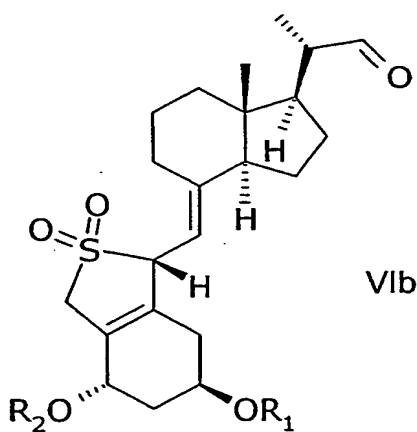
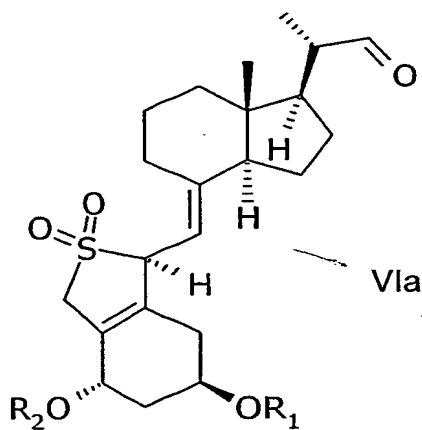
wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group, with the provisos that  $R_1$  and  $R_2$  cannot both be *tert*-butyldimethylsilyl, *tert*-butyldiphenylsilyl, or triisopropylsilyl; with the further proviso that when  $R_2$  is *tert*-butyldimethylsilyl,  $R_1$  cannot be *tert*-butyldiphenylsilyl.

32. A compound of general structure IIIb,



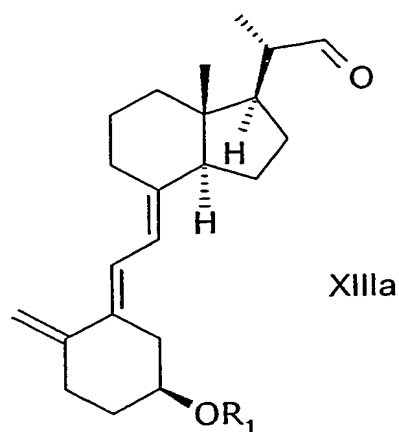
wherein  $R_1$  represents a hydroxy protecting group, and  $R_2$  represents hydrogen or a hydroxy protecting group; or  $R_1$  represents a hydrogen or a hydroxy protecting group, and  $R_2$  represents a hydroxy protecting group, except acetyl; with the proviso that  $R_1$  and  $R_2$  cannot both be *tert*-butyldimethylsilyl.

33. A compound of general structure VIa or VIb,



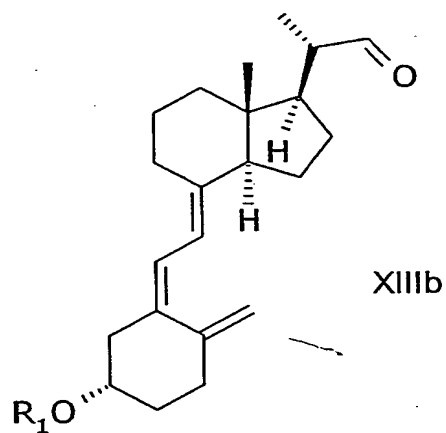
wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group, with the proviso that  $R_1$  and  $R_2$  cannot both be *tert*-butyldimethylsilyl.

34. A compound of general structure XIIIa,



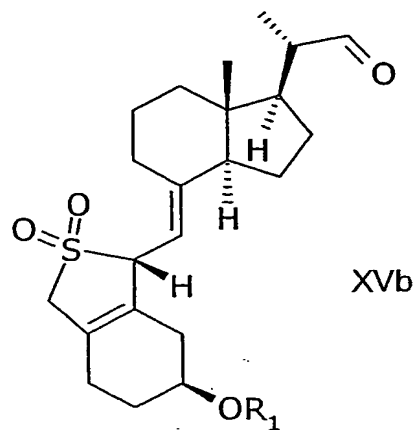
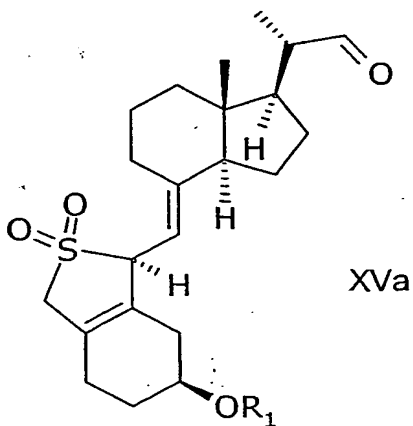
wherein  $R_1$  represents hydrogen or a hydroxy protecting group, except *tert*-butyldimethylsilyl.

- 5 35. A compound of general structure XIIIb,



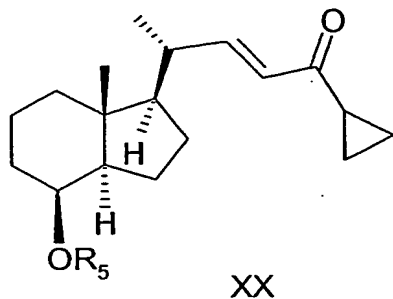
wherein  $R_1$  represents a hydroxy protecting group, except *tert*-butyldimethylsilyl.

36. A compound of general structure XVa or XVb,



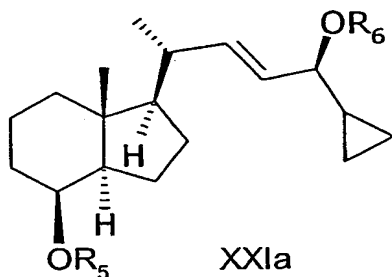
wherein  $R_1$  represents a hydroxy protecting group, except *tert*-butyldimethylsilyl, triisopropylsilyl, acetyl, or triethylsilyl.

37. A compound of general structure XX,



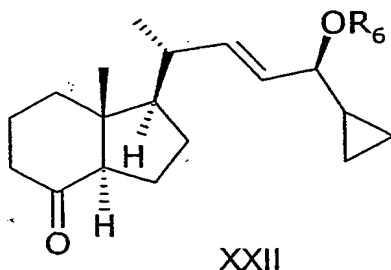
wherein  $R_5$  represents hydrogen or a hydroxy protecting group.

38. A compound of general structure XXIa,



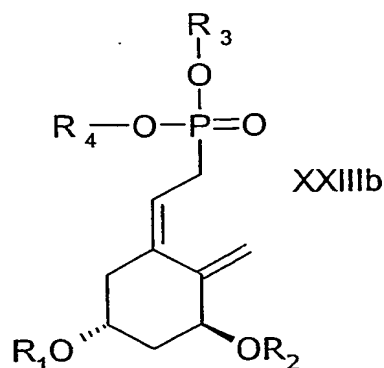
10       wherein  $R_5$  and  $R_6$  are the same or different and represent hydrogen or a hydroxy protecting group, with the provisos that when  $R_5$  is hydrogen  $R_6$  is not *tert*-butyldimethylsilyl, and when  $R_5$  is benzoate,  $R_6$  is not *tert*-butyldimethylsilyl or hydrogen.

15       39. A compound of general structure XXII,



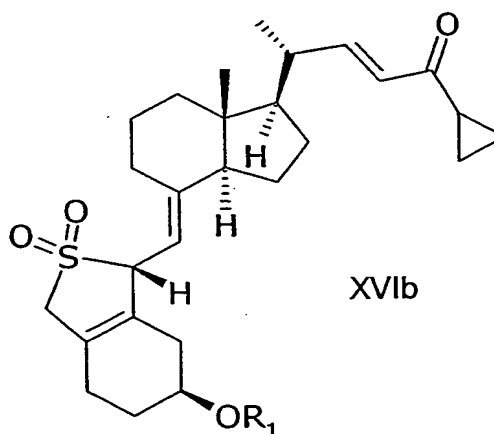
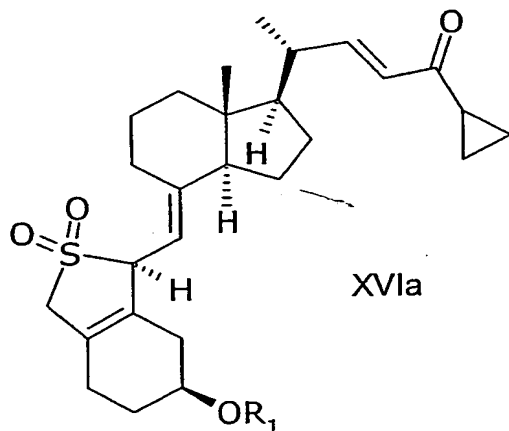
wherein  $R_6$  represents hydrogen or a hydroxy protecting group, except *tert*-butyldimethylsilyl.

20       40. A compound of general structure XXIIIb,



wherein  $R_1$  and  $R_2$  are the same or different and represent hydrogen or a hydroxy protecting group, and wherein  $R_3$  and  $R_4$  are the same or different and represent alkyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, or aryl, each being optionally substituted with one or more substituents selected from the group consisting of alkyl, aralkyl, cycloalkyl, cycloalkenyl, haloalkyl, hydroxyalkyl, alkenyl, alkynyl, aralkyl, aralkenyl, aralkynyl, aryl, oxo, alkoxycarbonyl, alkylcarbonyloxy, halogen, alkoxy, carboxy, sulfo or hydroxy.

41. A compound of general structure XVIa or XVIb,



wherein  $R_1$  represents hydrogen or a hydroxy protecting group.

42. Use of a compound according to any one of claims 26-41 as an intermediate in the manufacture of calcipotriol or calcipotriol monohydrate.

43. Use of (2-cyclopropyl-2-oxoethyl)phosphonic acid diethyl ester in the manufacture of calcipotriol.